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Farmer's Lung Disease

SUMMARY

Farmer's lung disease (FLD) is a hypersensitivity pneumonitis secondary to the inhalation of moldy hay spores. Its prevalence is likely underestimated despite the fact it may result in significant acute and chronic respiratory disability. The immunologic mechanisms are best explained as Gell and Coombs Type III & IV reactions. FLD is usually recognized by history and appropriate laboratory confirmation. Therapy requires removal of the patient from the offending antigens, although corticosteroids may be useful for constitutional symptoms. (Can Fam Physician 1982; 28:1817-1820).

SOMMAIRE

Le poumon de fermier est une pneumonite d'hypersensibilité secondaire à l'inhalation de spores de foin moisi. Sa prévalence est probablement sous-estimée, en dépit du fait que la maladie peut causer une invalidité respiratoire chronique et aiguë significative. Les réactions de type III et IV de Gell et Coombs fournissent la meilleure explication des mécanismes immunologiques. On reconnaît habituellement le poumon de fermier à l'histoire et on le confirme par des examens de laboratoire appropriés. La thérapie requiert d'éloigner le patient des antigènes offensifs, bien que les corticostéroïdes puissent être utiles pour les symptômes constitutionnels.

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IN 1713 RAMAZZINI observed severe respiratory disease following exposure to improperly dried, overheated grain dust.[1] Bjornsson wrote that his grandfather, an Icelandic farmer, suffered from "heymaedi" (hay shortness of breath) in the early 19th century.[2] In May 1932, J. M. Campbell, an observant county tuberculosis officer, described five cases of acute respiratory disease following exposure to moldy hay in the spring.[3] Later termed farmer's lung disease (FLD), this clinical entity has attained considerable importance in respiratory medicine.

FLD is a hypersensitivity reaction to organic antigens inhaled from moldy hay. It was the first hypersensitivity pneumonia (HSP) or extrinsic allergic alveolitis described; today it remains the most prevalent and best studied. FLD, unrecognized, can cause severe disability and death,[4] yet is often diagnosed by history alone and can be treated effectively by avoidance of moldy hay. Classically, it is manifested by fever, cough and dyspnea four to six hours after exposure and the pathological correlate is alveolar and interstitial inflammation of the lung.

Farmers are exposed to many organic antigens other than hay mold which can cause alveolitis. Two of these are moldy grain and chicken proteins. Although some include these under farmer's lung, we will use this term only in relation to hay.

Epidemiology

To understand the epidemiology of FLD, one has to know the antigen characteristics, since the antigen is the source of the disease. Improperly dried hay (greater than 30% moisture content) when stored in silos or stacked allows growth of micro-organisms and heat production.[5] This warm, damp environment causes thermophilic fungi to proliferate and sporulate beginning within one week and continuing for months to years. The lowest layers of hay contain the highest concentration of spores. Agitation may release white clouds of these respirable particles (0.5 u-1.3 u) into the air and cause disease in a susceptible host.

FLD is more prevalent in damper climates and is seen more often after a wet harvest season.[2] Peak incidence occurs in the late winter and early spring because the hay has had time to become moldy and the lower layers are being used for feed. In a Wisconsin study, dairy farmers with large herds were at higher risk.[6] Prosperous regions with increased automation might be expected to be associated with less exposure and a lower risk of disease, but this is not always the case.[6] The prevalence of FLD, established by questionnaire, is 9% among southern Manitoba cattle farmers.[7] In the United States rates among farming populations vary from 0.42% in Wisconsin to 3% in Wyoming.[6, 8] In Scotland 2.3-8.6% of farmers in varying regions have a history consistent with the disease.[2]

Prevalence rates, however, must be interpreted in the light of many factors. For example, there are no accepted diagnostic criteria and studies are usually done by questionnaire which may or may not include a physical exam and evaluation of serum precipitating antibodies.

Including women and children will lower observed prevalence rates, because they rarely develop FLD.[5, 9] Conversely, studying only adult male cattle farmers will increase the observed disease rates.

TABLE 1
Diagnosis of Acute FLD

Clinical setting
Farmer with lung disease
History
Symptoms 4-8 hours after moldy hay exposure, recurrence on re-exposure
Physical exam
Fever
Tachypnea
Inspiratory crackles
Chest X-ray
Non-specific infiltrates
Laboratory investigation
WBC $\leq$20,000
Low PaO_2*
Widened $PAO_2 - PaO_2$ difference**
Pulmonary function
Reduced FEV_1, VC and DLCO
Normal $\frac{FEV_1}{VC}$
Immunology
Serum antibodies
Bronchial challenge
Bronchioalveolar lavage
Lung biopsy
Granulomas and mononuclear cell infiltration

* Partial pressure of oxygen in arterial blood
** Ideal partial pressure of oxygen in alveoli

Clinical Presentation

FLD may present acutely in its classic form or as a chronic disease with insidious progression.

Classically, fever, malaise, dyspnea and cough develop four to eight hours after exposure to moldy hay. Cough is usually non-productive but purulent sputum has occasionally been reported.[10] Chills, headache and chest tightness may be present. Symptoms subside over days to weeks after exposure has ceased. Physical examination during an acute episode reveals tachypnea and tachycardia accompanied by a fever of 38-40°C. Bilateral crackles are frequently heard, but wheezing is present in less than 10% of cases. The white blood cell count is usually normal but may range up to 20,000 per mm,^{3} with a polymorphonuclear predominance.[5] Arterial blood gases may reveal hypoxemia and a widened alveolar-arterial gradient for oxygen tension. The chest X-ray is often normal.[11] When present, radiographic abnormalities are non-specific and include nodular mid-lung zone mottling, patchy acinar or interstitial infiltrates, and atelectasis. Only by obtaining a history of exposure to moldy hay or repeated episodes of similar symptoms can one differentiate this from a common infective pneumonia. If no clear-cut antigenic source can be elicited, it may be necessary to remove the patient from his usual environment and observe for resolution of his symptoms. The common course of acute disease is complete resolution although multiple attacks increase the risk of pulmonary fibrosis.[4]

The chronic course is frequently non-specific and difficult to recognize. Dyspnea progresses over many years, sometimes accompanied by malaise and weight loss. Auscultation of the chest reveals inspiratory crackles and the chest radiograph demonstrates a reticular pattern more commonly in the upper lung zones often associated with compensatory overinflation in other areas. A history of recurrent acute attacks may be interspersed in the chronic course. If not recognized as FLD and antigen exposure continues, 50% will become disabled within five years and 10% will eventually die from the disease.[4] When the disease is advanced, a small proportion will continue to deteriorate in spite of the inciting factor being removed.

Investigations

Pulmonary Function Testing

In both the acute and insidious disease, vital capacity (VC), forced expired volume in one second (FEV_1) and diffusing capacity (DLCO) are reduced. Airways obstruction with a reduction in the FEV_1 to VC ratio is infrequent but more common in chronic disease.

Immunology

The presence of serum precipitating antibodies to the antigens in moldy hay has been used as a marker for disease. Their presence indicates exposure and an immunological host response but they do not indicate active disease. Precipitins to micropolyspora faeni and thermoactinomyces vulgaris are most frequently associated with FLD. Many others, often in combination, have also been associated with FLD such as thermoactinomyces candidus and sacchari, aspergillus species and saccharamonospora viridis.[12]

Antibodies are found in 70-90% of FLD cases, but also in 6-20% of healthy farmers and 5% of office workers.[11] Antibody presence depends on the number of antigens searched for, the sensitivity of the technique and the host response. In summary, the presence of serum antibodies to antigens known to cause hypersensitivity pneumonitis are very helpful in supporting the clinical diagnosis, but not diagnostic in isolation and their absence does not exclude disease.

Skin testing with antigens found in moldy hay is not useful. It is not sensitive and false positive reactions occur because of a non-specific inflammatory response to the material.[13] Serum immunoglobulin E and total hemolytic complement are usually normal. Lymphocyte sensitization can be demonstrated by the ability to generate migration inhibition factor on exposure to the appropriate antigen. There is, however, overlap between healthy exposed people and those with FLD.[11] There is no known association between FLD

and serologically detectable HLA-A,B,C, foci antigens.[14]

Bronchial Challenge

When history and precipitating antibodies cannot establish the diagnosis, a positive bronchial challenge is considered proof of the disease.[5, 11] Williams demonstrated a positive response in 12 of 15 patients with FLD and in none of 20 controls.[15] To perform this test the subject inhales the suspected antigenic material, for example, an extract of M. Faeni or moldy hay dust, for 10-20 minutes. He is then observed frequently over the following 12 hours clinically, spirometrically and radiographically. Because the antigen dose for this test is not well standardized, severe reactions may occur with the potential for permanent tissue damage; alternatively a false negative reaction may occur. It is especially dangerous if pulmonary function is impaired before the test.

Bronchoalveolar Lavage

This procedure involves instilling fluid into bronchi through the bronchoscope and examining the subsequent aspirations for cellular and biochemical characteristics. Lavage is being extensively studied in assessing the activity of many interstitial lung diseases, assuming it reflects the inflammatory and immune cell population in the alveoli.[16] Lavage characteristics of hypersensitivity pneumonias include a high proportion of lymphocytes, most of which are T-cells and increased IgG and IgM to albumin ratios. These features differentiate HSP from other interstitial lung diseases, except sarcoidosis. However, this test is primarily a research tool at present and its role in diagnosing or managing FLD is not yet established.

Pathology

The acute phase of HSP is manifested by pulmonary alveolar wall and interstitial accumulation of neutrophils, mononuclear cells and edema. Obstructive bronchiolitis and capillary inflammation are frequently present. In the later stages of disease, mononuclear cells predominate and noncaseating granulomas are seen. Granulomas and inflammation eventually diminish and diffuse or localized non-specific interstitial fibrosis with architectural disruption of the lung characterize the end-stage of disease. There have been sporadic reports of celiac disease associated with FLD and one report of associated myopericarditis.[17, 18] With these exceptions, pathology is confined entirely to the lung.

Pathogenesis

FLD is described as a hypersensitivity reaction because of the many immunological phenomena present and the absence of organism invasion into tissue. Unfortunately it cannot be categorized under a single type of classic hypersensitivity reaction and each of the four types have been postulated to be involved. The acute disease is best explained by a type III Gell and Coombs[19] reaction as follows: Moldy hay antigens complex with antibodies in the lung, bind complement and attract neutrophils, which subsequently cause inflammation by release of their toxic enzymes and radicals. The chronic disease with mononuclear cell inflammation and granulomas is most consistent with a type IV cell-mediated immune reaction. A unifying hypothesis suggests sensitized pulmonary alveolar macrophages activated by antigen attract neutrophils and also modulate T cell activity leading to the appearance of mononuclear cells and granulomas.[11]

Differential Diagnosis

Acute FLD can only be differentiated from 'the flu' or infectious pneumonia by its temporal relation to moldy hay exposure or recurring episodes. Chronic progressive disease may be confused with non-specific interstitial fibrosis or even the progressive dyspnea due to cigaret-induced obstructive lung disease. History, presence of precipitins and a predominantly restrictive lung deficit should distinguish FLD.

Silo-fillers disease is an acute bronchiolitis resulting from inhalation of nitrogen oxides. Fresh silage generates nitric acid which, when exposed to air, produces nitrogen dioxide in high concentrations inside the silo for three to ten days. It can often be seen as a brown haze resting just above the silage. Inhalation leads to immediate cough, dyspnea and occasionally pulmonary edema. Initial symptoms resolve but may spontaneously recrudesce within a few weeks and either resolve or leave residual pulmonary insufficiency. Death is uncommon but can occur initially due to pulmonary edema or later as a result of bronchiolitis obliterans. Silo-fillers disease is not associated with mature silage or serum immune markers.

Intense dyspnea and pulmonary infiltrates without serological markers occurring within hours of massive exposure to moldy hay spores has been termed pulmonary mycotoxicosis.[20] It is difficult to be certain whether this is truly a toxic reaction to spores or acute FLD with non-identifiable antigens.

Farmers have an increased prevalence of wheezing, dyspnea and productive cough even when controlled for smoking habits.[21] Grain dust is one important cause of asthmatic symptoms manifested physiologically as a reduced FEV_1/VC. The particles may be physically irritating to the airways, but grain dust may also contain fungal spores, insecticides, mites and insect, animal and bacterial products. Grain molds less than hay occasionally cause hypersensitivity pneumonia.

Treatment

Avoidance of the offending antigen is the only known method of preventing disease. Acute disease is self-limiting and should be treated symptomatically with rest, supplemental oxygen and antipyretics. Prednisone 1 mg/kg/d may bring dramatic relief from severe constitutional symptoms, but its usefulness in chronic disease is not established.[11]

Educating farmers about the significance of respiratory symptoms may help identify disease in its reversible stages. The use of feed other than hay, mold inhibitors, and proper drying and ventilation of stored hay will reduce the number of spores produced. Portable respirators and masks with extremely fine pores are effective, but the former are cumbersome and the latter offer significant resistance to airflow, making physical labor difficult. Each case must be managed individually and if all else fails the patient will have to leave farming.

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